On page 32, please replace the paragraph beginning, "For native crystals from which the atomic structure coordinates of the invention are obtained, it has been found that sitting drops comprising about 1 µL of *H. pylori* LuxS polypeptide (5 mg/mL in 10 mM HEPES, pH 7.5, 150 mM sodium chloride..."with the following paragraph:

For native crystals from which the atomic structure coordinates of the invention are obtained, it has been found that sitting drops comprising about 1 µL of *H. pylori* LuxS polypeptide (SEQ ID NO: 1) (5 mg/mL in 10 mM HEPES, pH 7.5, 150 mM sodium chloride, 10 mM methionine, 1 mM beta-mercaptoethanol) with 1 µL reservoir solution (32% w/v PEG 1000, 200 mM ammonium sulfate, and 100 mM MES, pH 5.75) suspended over 0.5 mL reservoir solution for about one week at 20°C provide diffraction quality crystals. Similarly, sitting drops prepared by mixing about 1 µL of *D. radiodurans* LuxS polypeptide (SEQ ID NO:3) (19 mg/mL in 10 mM HEPES, pH 7.5, 150 mM sodium chloride, 10 mM methionine, 1 mM beta-mercaptoethanol) and 1 µL reservoir solution (26% w/v PEG monomethyl ether ("PEG MME") 5000, and 100 mM MES, pH 6.5) suspended over 0.5 mL reservoir solution for about one week at 4°C provide diffraction quality crystals. Sitting drops prepared by mixing about 1 µL of *H. influenzae* LuxS polypeptide (SEQ ID NO: 2) (10 mg/mL in 10 mM HEPES, pH 7.5, 150 mM sodium chloride, 10 mM methionine, 1 mM beta-mercaptoethanol) and 1 µL reservoir solution (21% w/v PEG MME 5000, and 100 mM Bis-Tris, pH 6.25) suspended over 0.5 mL reservoir solution for about one week at 12°C provide diffraction quality crystals.

On page 36, please replace the paragraph beginning, "LuxS crystals were also obtained from *H. influenzae* LuxS. The *H. influenzae* LuxS crystals, which may be native crystals..."with the following paragraph:

LuxS crystals were also obtained from *H. influenzae* LuxS (SEQ ID NO: 2). The *H. influenzae* LuxS crystals, which may be native crystals, heavy-atom derivative crystals or co-crystals, have a tetragonal unit cell and space group symmetry $P4_22_12$. In one form of crystalline *H. influenzae* LuxS, the unit cell has dimensions of a=129.59 +/- 1.3 Å, b=129.59 +/- 1.3 Å, c=53.74 +/- 0.5 Å. There are likely to be two LuxS molecules in the asymmetric unit, related by

an approximate 2-fold axis. The crystals appear as long (up to 0.4 mm), thin (typically 0.05 to 0.1 mm wide) rods.

On page 36, please replace the paragraph beginning, "LuxS crystals of the invention were also obtained from *D. radiodurans* LuxS. In one form, the *D. radiodurans* LuxS crystals, which may be native crystals..."with the following paragraph:

> LuxS crystals of the invention were also obtained from *D. radiodurans* LuxS (SEQ ID NO:3). In one form, the *D. radiodurans* LuxS crystals, which may be native crystals, heavy-atom derivative crystals or co-crystals, have a monoclinic unit cell and space group symmetry $P2_1$. The unit cell has dimensions of a=43.71 +/- 0.4 Å, b=82.18 +/- 0.8 Å, c=49.48 +/- 0.5 Å and beta = 102.78 +/- 1.0 degrees. There are likely to be two LuxS molecules in the asymmetric unit, related by an approximate 2-fold axis. The crystals appear as small blocks (typically 0.05 to .1 mm on a side). In another form of *D. radiodurans* LuxS crystals, a C2 monoclinic unit cell is observed with dimensions of a=51.19 +/- 0.5 Å, b=70.14 +/- 0.7 Å, c=49.73 +/- 0.5 Å and beta = 112.03 +/- 1.1 degree. There is one molecule of LuxS in the asymmetric unit.

On page 40, please replace the paragraph beginning, "The present invention provides, for the first time, the high-resolution three-dimensional structure and atomic structure coordinates of crystalline LuxS as determined by X-ray crystallography..."with the following paragraph:

> The present invention provides, for the first time, the high-resolution three-dimensional structure and atomic structure coordinates of crystalline LuxS as determined by X-ray crystallography. The specific methods used to obtain the structure coordinates are provided in the examples, *infra*. The atomic structure coordinates of four crystalline forms of LuxS are appended as Table 7, Table 8, Table 9, and Table 10 (*H. pylori* LuxS (SEQ ID NO: 1), *H. influenzae* LuxS (SEQ ID NO: 2), *D. radiodurans* $P2_1$ LuxS (SEQ ID NO: 3), and *D. radiodurans* LuxS (SEQ ID NO: 3) C2, respectively).

On page 41, please replace the paragraph beginning, "Examination of residual density after modeling of the LuxS protein revealed a patch of density near the metal binding site...."with the following paragraph:

Examination of residual density after modeling of the LuxS protein revealed a patch of density near the metal binding site. This was successfully modeled to be a methionine (see FIG. 11). This ligand was seen in both molecules in the asymmetric unit for *H. pylori* LuxS (SEQ ID NO: 1) and *H. influenzae* LuxS (SEQ ID NO: 2) and in one of the molecules (B) in *D. radiodurans* LuxS (SEQ ID NO:3) space group $P2_1$. Methionine was present in the polypepide solution used for crystallization in 10mM concentration, added to keep Se atoms reduced. Thus there is no indication that methionine plays an *in vivo* role as a substrate for LuxS. Indeed, its sidechain is too short to reach the metal site (see FIG. 11). However, through modeling with the program SPOCK (Christopher, 1998, Texas A & M University) it is apparent that there is considerable room for a larger amino acid to bind in this region. When S-ribosylhomocysteine, a proposed substrate for LuxS (PCT WO 00/32152), was modeled into the amino acid binding site several highly conserved residues of LuxS were identified as significant due to their closed proximity to this ligand: Ser 9, His 14, Arg 23, Asp 40, Arg 42, Glu 60, Met 84, Cyc 86, Thr 88, and Tyr 91.

On page 42, please replace the paragraph beginning, "Three crystalline LuxS polypeptides displayed a homodimer interaction in their asymmetric units, and the fourth, the *D. radiodurans* C2 crystalline polypeptide...."with the following paragraph:

Three crystalline LuxS polypeptides displayed a homodimer interaction in their asymmetric units, and the fourth, the *D. radiodurans* C2 crystalline polypeptide (SEQ ID NO:3), displayed a dimer with crystallographic symmetry. The dimerization is illustrated in FIG. 7. This dimerization was highly consistent between the three structures (alpha carbon superpositions of the dimers ranging from 1.0 Å^2 for *D. radiodurans* LuxS (SEQ ID NO: 3) $P2_1$ onto *H. influenzae* LuxS (SEQ ID NO: 2) to 1.2 Å^2 for *D. radiodurans* LuxS (SEQ ID NO: 3) $P2_1$ onto *H. pylori* LuxS (SEQ ID NO: 1) for residues 11-69, 77-118, and 125-152 of each monomer). The surface area buried through this interaction is 3930 Å^2 for the *D. radiodurans* $P2_1$ LuxS (SEQ ID NO: 3),

3,195 Å^2 for the *D. radiodurans* LuxS (SEQ ID NO: 3) C2 crystallographic dimer, 4160 Å^2 for *H. influenzae* LuxS (SEQ ID NO: 2), and 4180 Å^2 for *H. pylori* LuxS (SEQ ID NO: 1). These are very significant, comprising nearly a quarter of each molecules surface. Thus we propose that LuxS functions as a homodimer in solution. More evidence for this is the fact that the methionine ligand binding occurs at the dimer interface (see FIG. 7B) and a channel is provided for ligand entrance and exit through the opposing molecule (see FIG. 12).

On page 52, please replace the paragraph beginning, "The subsections below describe the production of a polypeptide containing the *H. pylori* LuxS protein...."with the following paragraph:

The subsections below describe the production of a polypeptide containing the *H. pylori* LuxS protein (SEQ ID NO: 1), and the preparation and characterization of diffraction quality crystals, heavy-atom derivative crystals.

On page 54, please replace the paragraph beginning, "The stereochemical quality of the atomic model was monitored using PROCHECK (Laskowski *et al.*, 1993, PROCHECK: a program to check the stereochemical quality of LuxS structures...."with the following paragraph:

The stereochemical quality of the atomic model was monitored using PROCHECK (Laskowski *et al.*, 1993, "PROCHECK: a program to check the stereochemical quality of LuxS structures," J. Appl. Cryst. 26:283-291). As defined in PROCHECK, for *H. pylori* LuxS (SEQ ID NO: 1), there are 87.7% (molecule A) and 86.2% (molecule B) of the residues in the model have main-chain torsion angles in the most favored Ramachandran regions . No residues fall in the disallowed region. In H. pylori, there are only two residues of molecule A and none of molecule B that fall in the generously allowed regions. The overall G-factor scores are 0.16 (*H. pylori*, molecule A) and 0.13 (*H. pylori*, molecule B).

On page 54, please replace the paragraph beginning, "The subsections below describe the production of a polypeptide containing the *H. influenzae* LuxS protein...."with the following paragraph:

> The subsections below describe the production of a polypeptide containing the *H. influenzae* LuxS protein (SEQ ID NO: 2), and the preparation and characterization of diffraction quality crystals, heavy-atom derivative crystals.

On page 55, please replace the paragraph beginning, "The MAD data was indexed and intergrated using the program Denzo and merged and scaled using the program Scalepack. The program SnB was then used to determine the location of Selenium-methionine ..."with the following paragraph:

> The MAD data was indexed and intergrated using the program Denzo and merged and scaled using the program Scalepack. The program SnB was then used to determine the location of Selenium-methionine Se's based on the peak wavelength data. These Se sites (12 of 14 were found) were refined and phase information for the protein obtained using the program SHARP. Solomon solvent flattening of the data was subsequently employed in SHARP. The resulting map was viewed in the program O and found to be of excellent quality with essentially all of both of the proteins in the asymmetric unit, main chain and sidechains, easily visible. This map was modeled using O to give the position of nearly all of the residues: residues 6 through 164 (molecule A) and 6 through 166 (molecule B) of *H. influenzae* LuxS (SEQ ID NO: 2). The model was refined using the program CNX.

On page 56, please replace the paragraph beginning, "The stereochemical quality of the atomic model was monitored using PROCHECK (Laskowski *et al.*, 1993, PROCHECK: a program to check the stereochemical quality of LuxS structures ..."with the following paragraph:

> The stereochemical quality of the atomic model was monitored using PROCHECK (Laskowski *et al.*, 1993, PROCHECK: a program to check the stereochemical quality of LuxS structures," J. Appl. Cryst. 26:283-291). As defined in PROCHECK, for *H. influenzae* LuxS (SEQ ID NO: 2) there are 92.8% (molecule A) and 90.8% (molecule B) of the residues in the model have main-chain torsion angles in the most favored Ramachandran regions . There

is only one residue that falls in the disallowed region (H. Influenzae, molecule B). H. influenzae has one residue of each molecule falling in the generously allowed regions. The overall G-factor scores are 0.25 (*H. influenzae*, molecules A and B).

On page 56, please replace the paragraph beginning, "The subsections below describe the production of a polypeptide containing the *D. radiodurans* LuxS protein ..."with the following paragraph:

> The subsections below describe the production of a polypeptide containing the *D. radiodurans* LuxS protein (SEQ ID NO:3), and the preparation and characterization of diffraction quality crystals, heavy-atom derivative crystals.

On page 58, please replace the paragraph beginning, "The subsections below describe the production of a polypeptide containing the *D. radiodurans* LuxS protein ..."with the following paragraph:

> The subsections below describe the production of a polypeptide containing the *D. radiodurans* LuxS protein (SEQ ID NO:3), and the preparation and characterization of diffraction quality crystals, heavy-atom derivative crystals.

IN THE CLAIMS

Marked up versions of the following amended claims are attached hereto as Exhibit B.

Please amend claims 2, 24, 33, 46, and 51 to read as follows:

2. (Amended) The crystal of Claim 1 wherein the LuxS is *H. pylori* LuxS (SEQ ID NO: 1), LuxS, *H. influenzae* LuxS (SEQ ID NO: 2) or *D. radiodurans* LuxS (SEQ ID NO:3).

24. (Amended) The method of Claim 23 wherein the LuxS polypeptide is *H. pylori* LuxS polypeptide (SEQ ID NO: 1), *H. influenzae* LuxS polypeptide (SEQ ID NO: 2) or *D. radiodurans* LuxS polypeptide (SEQ ID NO:3).